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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,537	08/24/2001	Brian Seed	00786/247003	3555

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

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16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,537	SEED ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A Notice of Withdrawal from Issuse under 37 CFR 1.313(b) was mailed July 14, 2004 to allow entry of the rejections set forth below.

Status of Claims

2. Claims 22-30 are pending and currently under examination.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 23-24 and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 requires the extracellular portion of the claimed proteinaceous chimera receptor to further comprise the IgG1 hinge, CH3 and CH3 domains having a particular sequence, wherein the sequence recited within the claim is not an amino acid sequence. SEQ ID NO: 32, as recited in claim 26 is a nucleotide sequence. This additional requirement differs from the main invention—a proteinaceous chimera receptor. Ergo, due to this discrepancy noted, it is unclear if Applicant intends to recite SEQ IDNO: 33, the protein encoded by SEQ ID NO: 32.

Claims 23-24 and 27-28 recite the limitation CD4 "portion" in line 1 of each respective claim. There is insufficient antecedent basis for this limitation in the claim.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 22-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed a proteinaceous chimera receptor that comprises three distinct components:

i) an extracellular portion which includes a CD4 domain that specifically recognizes and binds HIV or an HIV-infected cell but not does not mediate HIV infection,

ii) a transmembrane portion, and

iii) an intracellular portion.

The extracellular portion which includes a CD4 domain that specifically recognizes and binds HIV or an HIV-infected cell but not does not mediate HIV infection lacks adequate written description. The claims comprises a negative limitation that excludes CD4 domains that mediate HIV infection. However, the specification does not implicitly or inherently teach of CD4 domains that do not mediate HIV infection. The specification does not teach which CD4 domain(s) that are capable of performing the function that is required of the CD4 component of the instantly claimed invention. It is noted that the specification teaches that a chimera that comprises the first two domains (D1-D2) of CD4, and all four domains of CD4 were impervious to HIV-induced syncytia

formation. However, no teaching can be found within the specification with regard to which specific CD4 domain(s) should be present or excluded from the instantly claimed invention.

Applicant is either required to point to adequate support for the required CD4 domains that do not mediate HIV infection or cancel the limitation that is not supported by the disclosure.

7. Claims 22-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling for an isolated proteinaceous chimera receptor comprising an extracellular portion which includes a CD4 domain, a transmembrane portion, and an intracellular portion which signals a cell bearing said receptor to destroy a receptor-bound HIV or HIV infected cell, wherein said CD4 domain is separated by the transmembrane by either an alpha helix or the IgG1 hinge, CH2 and CH3 domains at a distance that is sufficient for said CD4 domain to specifically recognizes and binds to HIV or an HIV-infected cell but does not mediate HIV infectivity.

The specification does not reasonably provide enablement for a proteinaceous chimera receptor, said receptor comprising (a) an extracellular portion which includes a CD4 domain that specifically recognizes and binds HIV or an HIV-infected cell but which does not mediate HIV infection, (b) a transmembrane portion, and (c) an intracellular portion which signals a cell bearing said receptor to destroy a receptor-bound HIV or HIV-infected cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

There are two aspects to the instant enablement rejection. The first is directed at the first component of the claimed invention, an extracellular portion that includes a CD4 domain that specifically recognizes and binds HIV or an HIV infected cell but does not mediate HIV infection. The second aspect is based on the grounds that a disclosed critical limitation is missing from a claim, based on the teaching in the specification concerning the distance criticality between the CD4 domains and cell membranes.

The nature of the claimed invention is directed at a chimera receptor that serves as a decoy for HIV and defers HIV infectivity by attaching to HIV or HIV infected cells and destroys the receptor bound HIV or HIV infected cells.

The prior art teaches that CD4 consists of four immunoglobulin like domains. The first domain on the CD4 is the binding site for gp120 and the side chains of residues lys-35, Phe-43, and Arg-59 on the D1-D2 domain on the CD4 that are in direct interaction of gp120[1]. While this portion of CD4 is known to bind gp120, the prior art does not teach a CD4 domain that does not mediate HIV infection.

The specification teaches that the fusion of D1-D4 domains of the CD4 with the zeta chain of the TCR was able to mediate syncytia formation. The specification teaches that CD4(D1-D2):Ig:CD7 and CD4(D1-D4):Ig:CD7 chimera gave no sign of cell fusion, insusceptible to HIV-induced syncytia formation. However, the specification does not teach which CD4 domains specifically recognize and bind to HIV or an HIV infected cell but do not mediate HIV infection. Hence, from the teaching of the prior art and the specification, one skilled in the art would not be able to determine which CD4 domains to use or not use with the instantly claimed invention, wherein the claimed invention requires that extracellular domain includes a CD4 portion that specifically recognizes and binds HIV or an HIV infected cell but does not mediate HIV infection.

Regarding the second aspect of the instant enablement rejection, the specification teaches that it is the physical distance between the extracellular domain of

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[1] Wu et al., Kinetic and structural analysis of mutant CD4 receptors that are defective in HIV gp120 binding, Proc. Natl. Acad. Sci. USA, 1996, 93: 15030-15035.

the CD4 molecule and the lipid bilayer that confers the ability to resist HIV infection, see lines 22-25 of page 56. The specification teaches that receptors that comprises the attachment CD4 to either a synthetic alpha helix or an the hinge do not mediate HIV infectivity, whereas, CD4 molecules that lacks such attachment has demonstrated to mediate HIV infectivity, see Table 1 on page 58 of the specification. Specifically, the specification discloses that the distance in which the CD4 domains of the extracellular portion of the chimera receptor project itself from the cell membrane is critical to infectivity of HIV. The specification teaches that the "extracellular domains of CD4 should optimally be projected away from the cell membrane by at least 48 angstroms" to resist HIV-1 infectivity, lines 20-24 of page 60 in the instant specification. However, such criticality is not recited in the claims, with the exception of claims 26-28. Currently, as written, the breadth of the claims encompass chimeric receptors that comprises an extracellular portion, wherein the distance in which the extracellular portion projects away from a cell membrane is limitless. Because the specification notes that the distance between CD4 domain(s) and the cell membrane is critical in the ability of the CD4 domains to resist HIV infection, the claims are rejected under U.S.C 112, 1st paragraph for not enabling under the guidance of MPEP 2164.08(c), Critical Feature Not Claimed. MPEP 2164.08(c) states that [a] feature which is taught as critical in a specification and is not recited in the claims should result in a rejection of such claim under the enablement provision section of 35 U.S.C. 112. See In re Mayhew, 527 F.2d 1229, 1233, 188 USPQ 356, 358 (CCPA 1976). In determining whether an unclaimed feature is critical, the entire disclosure must be considered. Features which are merely

preferred are not to be considered critical. In re Goffe, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976). Limiting an applicant to the preferred materials in the absence of limiting prior art would not serve the constitutional purpose of promoting the progress in the useful arts. Therefore, an enablement rejection based on the grounds that a disclosed critical limitation is missing from a claim should be made only when the language of the specification makes it clear that the limitation is critical for the invention to function as intended. Broad language in the disclosure, including the abstract, omitting an allegedly critical feature, tends to rebut the argument of criticality. In view of the MPEP 2164.08(c), the claimed invention, with the exception of claims 26-28, are rejected for not being enabling because the claims do not recite the limitation that the instant specification regards as critical to the claimed invention.

In summation, due to the lack of teaching from the prior art and the specification with regards to CD4 domains that recognizes and binds to HIV or HIV infected cells but do not mediate HIV infection, and the disclosure concerning the criticality of the distance between the CD4 domain(s) and cell membranes in resisting HIV infection and absence of such criticality in the claims, the amount of experimentation that would be imposed upon one skilled in the art would be an undue burden.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 22, 25 and 29-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 5,843,728. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same invention.

Both set of claims are directed to a protein chimera receptor comprising i) an extracellular CD4 portion which recognizes and binds HIV or an HIV infected cell; ii) an

intracellular portion, wherein the intracellular portion which is capable of signaling the therapeutic cell to destroy the receptor-bound HIV-infected cell; and iii) a transmembrane domain, wherein the transmembrane domain is the transmembrane portion of CD7; and wherein the receptor does not mediate HIV infection.

The difference between the two set of claims is that claim 10 of the '728 patent does not

i) contain a functional requirement for the intracellular portion. However, the '728 specification discloses that the intracellular portion is capable of signaling the therapeutic cell to destroy the receptor-bound HIV-infected cell.

ii) limit the extracellular domain to CD4. However, the '728 specification teaches the use of CD4 to attract HIV. Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use CD4 to attract HIV.

iii) limit the transmembrane portion to the transmembrane of CD7. However, the '728 specification teaches the use of the transmembrane of CD7 as the transmembrane portion. Ergo, it would have been prima facie obvious for one of ordinary skill in the art to use the transmembrane CD7 as the transmembrane portion of the claimed invention.

iv) contain a functional requirement for the receptor, such as does not mediate infectivity, and destroys receptor-bound HIV or HIV infected cell. However, the '728 specification teaches that the receptor is capable of both functions, not mediate infectivity and destroy receptor-bound HIV or HIV infected cell.

10. Claim 22 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,392,013.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same invention.

Both set of claims are directed to a protein chimera receptor comprising i) an extracellular CD4 portion which recognizes and binds HIV or an HIV infected cell; ii) an intracellular portion, wherein the intracellular portion which is capable of signaling the therapeutic cell to destroy the receptor-bound HIV-infected cell; and iii) a transmembrane domain; and wherein the receptor does not mediate HIV infection.

The difference between the two set of claims is that claims 1-5 of the '013 patent does not

i) contain a functional requirement for the intracellular portion. However, the '013 specification discloses that the intracellular portion is capable of signaling the therapeutic cell to destroy the receptor-bound HIV-infected cell.

ii) limit the extracellular domain to CD4. However, the '013 specification teaches the use of CD4 to attract HIV. Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use CD4 to attract HIV.

11. Claims 22-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-14 of U.S. Patent No. 6,753,162. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the same invention.

Both set of claims are directed to a protein chimera receptor comprising i) an extracellular CD4 portion which recognizes and binds HIV or an HIV infected cell; ii) an intracellular portion, wherein the intracellular portion which is capable of signaling the

therapeutic cell to destroy the receptor-bound HIV-infected cell; and iii) a transmembrane domain; and wherein the receptor does not mediate HIV infection.

The difference between the two set of claims is that claims 13-14 of the '162 patent does not

i) contain a functional requirement for the intracellular portion. However, the '162 specification discloses that the intracellular portion is capable of signaling the therapeutic cell to destroy the receptor-bound HIV-infected cell.

ii) define the CD4 portion. However, the '162 specification teaches the use of amino acids 1-394 of SEQ ID NO: 29 and amino acids 1-200 of SEQ ID NO: 31 as the CD4 portion.

iii) claim 13 does not require the addition of a hinge, CH3, and CH2 domains of the human IgG1 molecule of SEQ ID NO: 33. However, the '162 specification teaches the addition of the hinge to the chimera receptor leads to a chimera that is capable of resisting syncytium formation. Ergo, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to include a hinge to the chimera receptor.

iv) the CD4 portion is projected away from the membrane of a cell bearing said receptor by at least 48 and 72 angstroms. However, the '162 specification teaches that the extracellular domains of CD4 should optimally be projected away from the cell membrane by at least 48 angstroms, and preferably by at least 72 angstroms in order to resist HIV-1 infection. Ergo, it would have been prima facie obvious for one of ordinary

skill in the art at the time the invention was made to project the CD4 portion by at least 48 and 72 angstroms away from the membrane of a cell bearing said receptor.

v) limit the intracellular portion to a T cell receptor protein, particularly ζ; B cell receptor protein, or an Fc receptor protein. However, the '162 specification teaches that all of the listed proteins can be used as the intracellular portion. Ergo, it would have been prima facie obvious for one of ordinary skill in the art to use any one of the intracellular portions described in the specification.

vi) claim 14 does not limit the transmembrane domain to the CD7 transmembrane domain of SEQ ID NO: 35. However, the '162 specification teaches that the transmembrane domain can be the CD7 transmembrane domain of SEQ ID NO: 35. Ergo, it would have been prima facie obvious for one of ordinary skill in the art to use the CD7 transmembrane domain of SEQ ID NO: 35 as the transmembrane domain of the claimed invention.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E.Le

JEFFREY PARKER
PRIMARY EXAMINER